

AN ATYPICAL PRESENTATION OF DIABETIC MYONECROSIS

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ABSTRACT

Objective: Diabetes myonecrosis, also called diabetic muscle infarction (DMI), is a rare complication of diabetes. Given its rarity, our understanding of the underlying causes or the optimal management of DMI cases remains unclear.

Methods: We report on a patient who experienced 2 episodes of DMI and we also review the literature.

Results: A 46-year-old male with longstanding type 2 diabetes mellitus with multiple microvascular complications presented with acute-onset painful right thigh induration. On physical examination, he had right thigh swelling, tenderness, and crepitus. Blood tests showed leukocytosis, elevated creatine phosphokinase, and elevated acute-phase reactants. Microbiological cultures were negative. Glycated hemoglobin was 6.4% (46 mmol/mol). Magnetic resonance imaging demonstrated T2 hyperintensity involving the quadriceps group. The clinical and laboratory signs suggested a muscle infection. A muscle biopsy was sugges-

tive of DMI. Eleven months later, the patient presented again with a 4-week history of left thigh pain and weakness in both legs. On examination, he had bilateral thigh anterior tenderness without evidence of swelling or induration. He also had marked bilateral proximal motor deficiency and inability to stand or ambulate. Despite a different clinical presentation, imaging features were consistent with DMI. The patient was managed with conservative therapy. His strength improved significantly after 3 months of follow up.

Conclusion: The typical clinical presentation of DMI includes unilateral acute-onset pain in the quadriceps, local swelling, and the appearance of a palpable painful mass. The second episode in our patient illustrates an atypical clinical presentation of DMI and shows the importance of the correlation of clinical and imaging findings for the diagnosis of DMI. (AACE Clinical Case Rep. 2019;5:e77-e81)

Abbreviations:

DA = diabetic amyotrophy; **DMI** = diabetic muscle infarction; **HbA1c** = hemoglobin A1c; **MRI** = magnetic resonance imaging

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INTRODUCTION

A variety of musculoskeletal conditions are associated with diabetes mellitus including diabetes myonecrosis, also called diabetic muscle infarction (DMI), which is a rare and probably underdiagnosed diabetes-related condition (1). We report a case of a patient with 2 episodes of DMI, the second of which showed an atypical clinical presentation. In addition, we review the clinical characteristics, laboratory findings, imaging findings, treatments, and prognostic evolution of the disease.

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CASE REPORT

A 46-year-old male with a 20-year history of type 2 diabetes mellitus and multiple microvascular complications including proliferative retinopathy, distal polyneuropathy in both feet, chronic kidney disease stage 4, and autonomic dysfunction (erectile dysfunction, chronic diarrhea) presented with a 10-day history of anterior right thigh induration and acute-onset pain. He denied history of trauma or fever.

On physical examination, blood pressure was 183/93 mm Hg, heart rate 92 bpm, and temperature was 36.8°C. Right thigh edema, tenderness, and crepitus in the anterior compartment were noted on physical exam. Distal pulses were palpable. Blood tests showed signs of systemic inflammation including leukocytosis (15,100 cells/mm³) with neutrophilia (83%), elevated erythrocyte sedimentation rate (120 mm) and elevated C-reactive protein (12.92 mg/dL). The patient was anemic with hemoglobin of 8.7 g/dL and also had elevated creatinine (6.3 mg/dL), blood urea nitrogen (82 mg/dL), and creatine phosphokinase (1,180 U/L). Hemoglobin A1c (HbA1c) was 6.4% (46 mmol/mol). Blood cultures were negative.

A doppler ultrasound of the right leg was negative for deep vein thrombosis. Magnetic resonance imaging (MRI) without contrast demonstrated diffuse T2 hyperintensity consistent with myositis involving the vastus intermedius, vastus lateralis, adductor magnus, and rectus femoris muscles as well as circumferential subcutaneous edema. Fasciitis could not be excluded due to the lack of fat suppression (Fig. 1 A and B). Due to suspicion of necrotizing fasciitis, decompressive fasciotomy of the anterior compartment with debridement was performed and showed edematous soft tissue, viable muscle, and no purulence. No bacterial growth was found in tissue cultures. The diagnosis of DMI was confirmed by biopsy of the right quadriceps group that demonstrated necrotic, acutely inflamed

muscles (Fig. 2 A and B). The treatment consisted of analgesia, low-dose acetylsalicylic acid, and bed rest. After 19 days the patient was transferred to a rehabilitation center and recovered completely 2 months later.

Eleven months later, the patient presented with a second episode of DMI. He reported a 4-week history of anterior left thigh pain and weakness in both legs, without previous trauma or other symptoms including fever. Physical examination revealed blood pressure of 150/79 mm Hg, heart rate 75 bpm, temperature 37.1°C, left thigh anterior tenderness, and marked bilateral proximal motor deficiency with the inability to stand or walk. Blood tests showed potassium of 5.6 mEq/L, creatinine 6.0 mg/dL, glomerular filtration rate 12 mL/min/1.73 m², blood urea nitrogen 52 mg/dL, and hemoglobin 11.4 g/dL. HbA1c was 6.4% (46 mmol/mol). Blood cultures were negative.

The diagnosis of DMI was confirmed by MRI without contrast with axial T2-weighted short-tau inversion recovery images that demonstrated edema most notably within the left quadriceps group and, to a lesser extent, within the sartorius. No obvious abnormality was detected along the course of the sciatic, femoral, or obturator nerves (Fig. 1 C). Treatment consisted of analgesia, low-dose acetylsalicylic acid, and bed rest. After 2 weeks of hospitalization the patient was transferred to a rehabilitation center. The treatment was focused on tight control of cardiovascular risk factors. Three months later the patient's strength improved moderately.

DISCUSSION

Diabetic myonecrosis or DMI, first reported in 1965 (2,3), is a rare complication associated with poorly controlled diabetes mellitus and multiple microvascular complications (Table 1). A systematic review was published in 2015 looking at 126 patients and 170 episodes

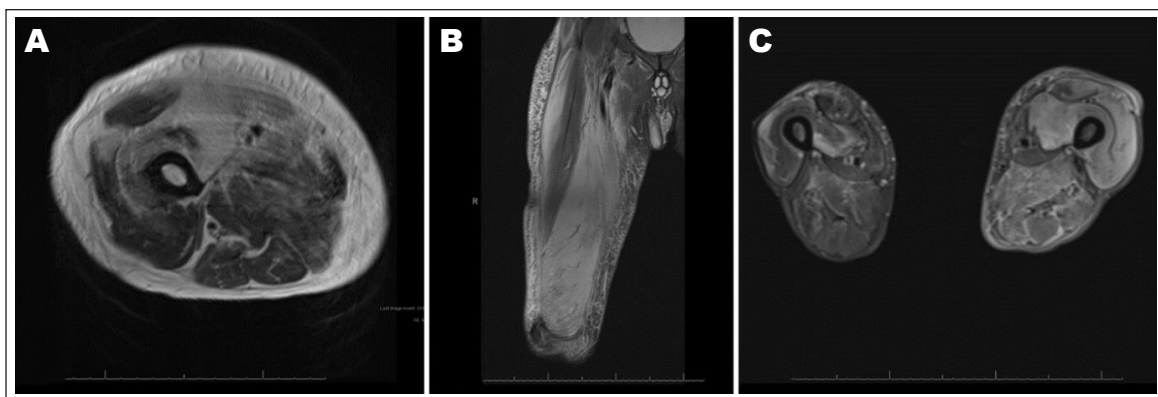


Fig. 1. Magnetic resonance images. Axial images of right leg (A) demonstrating diffuse T2 hyperintensity consistent with myositis with significant involvement of the vastus intermedius, vastus lateralis, adductor magnus, and rectus femoris in the first episode. Coronal short-tau inversion recovery images (B) could not determine well the intramuscular fascial planes due to the lack of fat suppression and therefore fasciitis could not be excluded in the first episode. Axial T2-weighted short-tau inversion recovery images (C) of both lower extremities demonstrated edema within the left quadriceps group, and no obvious abnormality along the course of the bilateral sciatic nerves, bilateral femoral nerves, or bilateral obturator nerves was demonstrated in the second episode.

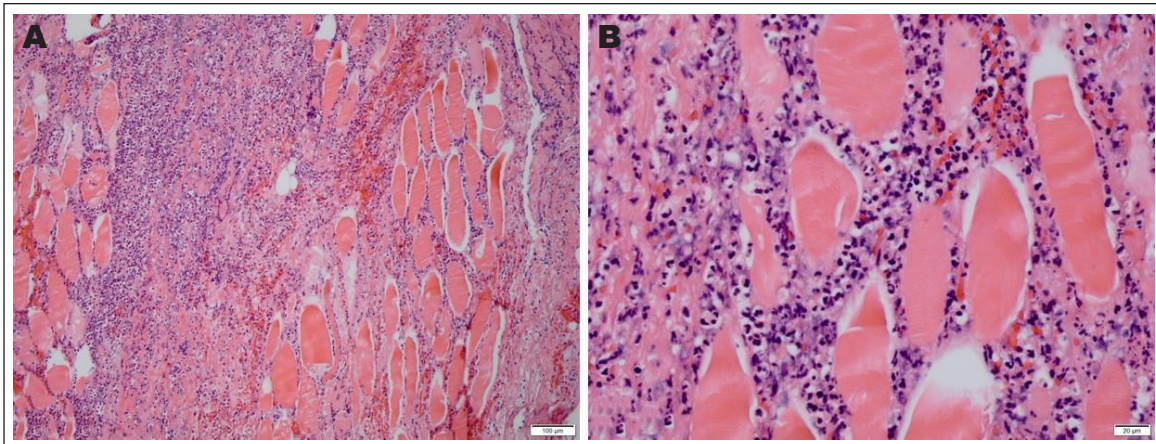


Fig. 2. Medium magnification of a biopsy from the right lower extremity medial thigh muscle (A). The skeletal muscle is severely damaged and necrotic. The destructive process is advanced and the differential histopathologic diagnosis is broad and includes pyogenic infectious such as necrotizing myofasciitis, vascular compromise, compartment syndrome, and toxic/metabolic injury. Hematoxylin and eosin stain; $\times 10$. High magnification of the same tissue fragment (B) better demonstrates skeletal muscle destruction. Here, fragmented skeletal muscle is surrounded and destroyed by severe, acute inflammatory exudate. Hematoxylin and eosin stain; $\times 40$.

of DMI (1). It found that DMI is more frequent in women, occurs in both type 1 and 2 diabetes mellitus, and that its typical clinical presentation includes acute-onset pain in the affected muscle (most commonly in the quadriceps), local swelling, and the posterior appearance of a palpable painful mass. Previous trauma or fever is unusual. Bilateral affection occurs in $<33\%$ of cases (1,3-5). The pathophysiology of DMI remains unclear but seems related to vasculopathic changes associated with longstanding and poorly controlled diabetes.

The differential diagnosis of DMI includes urgent medical conditions like bacterial infections, deep vein thrombosis, intramuscular hematoma, and uncommon conditions like tumors, calciphylaxis, polymyositis, and diabetic amyotrophy (DA) (4-7). Diabetic lumbosacral radiculoplexus neuropathy or DA is a rare complication that affects $<1\%$ of diabetes patients (8,9). Likewise, DMI is a rare diabetes-related condition that shares some clinical features with DA observed during the second episode in our patient. Consequently, DA was considered in the differential diagnosis in our patient. The diagnosis is based on the presence of a compatible clinical presentation, with electrophysiologic studies excluding myopathy and lumbosacral imaging excluding compressive etiologies (10,11). In DA, MRI typically shows increased T2 signal in the affected nerve or plexus in most patients and, in some cases, muscle edema or atrophy (12).

There are no specific laboratory or radiologic markers for DMI (1,3,4) (Table 2). MRI is the most valuable diagnostic technique, as it enables the exclusion of other conditions. The characteristic features of DMI in MRI include an increased signal from the affected muscle area (intramuscular and perimuscular tissues) in T2-weighted, inversion-recovery, and gadolinium-enhanced images. Isointense or hypointense areas on T1-weighted images, secondary

to edema and inflammatory changes associated with the infarction are also common (5,6,13,14). Muscle biopsy can provide a definitive diagnosis by showing muscle necrosis and edema, but it is currently discouraged and it is reserved for patients in whom a rapidly progressive infection of the muscle or fascia cannot be excluded as with our patient during the first episode (1,3,5,13).

Treatment recommendations for DMI include rest, optimal glycemic control, analgesia, and low-dose acetylsalicylic acid. An observational study suggests that nonsteroidal anti-inflammatory drug treatment may improve recovery. In general, the short-term prognosis of DMI is good, resolving spontaneously over a few weeks. Average recovery times from treatment onset were 5.5, 8, and 13 weeks for patients treated with nonsteroidal anti-inflammatory drugs, bed rest with analgesics, and surgical resection, respectively. However, recurrence is frequent and usually involves different muscles (1,3,4).

CONCLUSION

DMI is a rare complication of diabetes mellitus related to microangiopathic changes that lead to muscle infarct. There is no clear consensus on diagnostic criteria or management of this condition. Our case demonstrates that rare diabetic complications such as DMI may have an atypical clinical presentation and underlines the importance and limitations of isolated clinical and imaging findings. For patients with longstanding diabetes mellitus and known microvascular complications that present with acute pain and proximal lower extremity weakness that worsens over days or weeks without any prior history of trauma, the findings on MRI of increased T2 signal, muscle enlargement, and subcutaneous and subfascial edema without nerve or plexus involvement favor the diagnosis of DMI.

Table 1 Characteristics and Clinical Presentation of Diabetic Myonecrosis*	
Prevalence	Very rare
Pathophysiologic mechanism	Not well described. Proposed to be related to atherosclerosis, diabetic microangiopathy, vasculitis with thrombosis, and ischemia-reperfusion injury.
Sex	Women: 54-61.5%
Mean age at presentation	T1DM: 36 years; T2DM: 52 years
Duration of diabetes at onset	T1DM: 19 years; T2DM: 11 years
Hemoglobin A1c at diagnosis	9%
History of diabetes complications	93% of cases Nephropathy: 70-80% Retinopathy, nephropathy, and neuropathy: 45%
Clinical presentation: Pain Swelling Muscle weakness Others	80% 76% Usually not present Palpable masses: 34%; fever: 11%
Location in lower extremities	Proximal: 83.7%; distal: 15-19%
Upper extremity involvement	Rare
Bilateral symptoms	8-33%
Abbreviations: T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus. *Values are shown as mean percentages or years.	

Table 2 Laboratory, Imaging Tests, Treatments, and Evolution of Diabetic Myonecrosis*	
Laboratory features: elevated CRP elevated ESR elevated CPK leukocytosis	90% 53-83% 32-48% 8-42%
Imaging tests	Ultrasound: well-marginated, hypoechoic intramuscular lesion. MRI: increased signal in T2-weighted, inversion-recovery, and gadolinium-enhanced images and isointense or hypointense areas on T1-weighted images. Nerves and plexus preserved.
Other tests	Muscle biopsy: muscle necrosis and edema.
Diagnosis	1) Typical clinical and MRI features. 2) Laboratory and imaging studies exclude other disorders. 3) Muscle biopsy when infection or malignant tumor cannot be excluded.
Treatment	Rest, optimal glycemic control, analgesia, and low-dose acetylsalicylic acid.
Prognosis	Resolution over a few weeks to months. Mortality rate: 10% within 2 years.
Recurrence	35-48% (of which 39-61% involve another muscle)
Abbreviations: CPK = creatine phosphokinase; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; MRI = magnetic resonance imaging. *Values are shown as mean percentages or years.	

DISCLOSURE

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